CASE REPORT

Myeloma associated amyloidosis presenting as subacute liver failure

T J S Cross, J A Wendon, A Quaglia, J R Salisbury, M A Heneghan, P M Harrison

Postgrad Med J 2006;**82**:e13 (http://www.postgradmedj.com/cgi/content/full/82/969/e13). doi: 10.1136/pgmj.2006.044883

Multiple myeloma related amyloidosis is rare and its presentation with subacute liver failure (SALF) has not been reported. A case is described of a 46 year old woman presenting with a six week history of nausea, abdominal pain, and jaundice. Routine tests failed to establish a cause. Computed tomography showed a small volume liver consistent with SALF. Emergency liver transplantation was not undertaken because of the suspicion of underlying malignancy. At necropsy, liver biopsy showed amyloid deposition and bone marrow biopsy showed multiple myeloma. Thus, amyloidosis should be added to the list of potential causes of SALF.

Acute liver failure (ALF) is defined as the onset of hepatic encephalopathy within four weeks of the development of jaundice in a patient without a previous history of chronic liver disease. In subacute liver failure (SALF), hepatic encephalopathy occurs between 28 days and 72 days after the onset of jaundice.[1] The development of liver failure as a presenting feature of a malignancy is rare.[2] We report on a 46 year old woman who developed SALF presenting with anorexia, jaundice, and abdominal pain resulting from multiple myeloma related amyloidosis. To our knowledge, this is the first such case to have been described.

CASE REPORT

A 46 year old white woman presented to her local hospital in April 2005 with a one week history of generalised abdominal pain and jaundice. She had felt unwell for six weeks with anorexia and vomiting. She was previously healthy, and described no weight loss. On examination, she was not encephalopathic. Spider naevi were present, and she was jaundiced. Abdominal examination showed small volume ascites. She had a temperature of 37.3℃. Cardiovascular, respiratory, and neurological examinations were normal. The clinical concern was that this might represent Budd-Chiari syndrome and therefore, she was transferred to a tertiary liver centre.

On arrival a liver ultrasound showed normal patent vessels. Serological tests for hepatitis A, B, and C viruses, cytomegalovirus, Epstein-Barr virus, autoimmune hepatitis, Wilson's disease, and a prothrombotic screen were all negative. In addition, a transthoracic echocardiogram showed normal left and right ventricular function. Computed tomography of the chest, abdomen, and pelvis showed a small volume liver with changed perfusion, consistent with SALF. There were no mass lesions, or lymphadenopathy.

A 24 hour urinary collection was performed in view of dipstick testing showing proteinuria. This showed a creatinine clearance of 62 ml/min and a 24 hour urinary protein loss of 7.4 g/24 h (NR <250 mg/24 h). Her condition deteriorated on day 18 because of sepsis, and she was transferred to the liver intensive therapy unit. Laboratory studies showed: haemoglobin of 106 g/l (normal range NR 115–155), platelets 109×10^9/l (NR 150–450), white cell count 11×10^9/l (NR 4–11), sodium 151 mmol/l (NR 135–145), urea 4.9 mmol/l (NR 3.5–8), creatinine 106 mmol/l (NR 45–120), corrected calcium 3.14 mmol/l (NR 2.2–2.6), bilirubin 345 μmol/l (NR 3–17), aspartate aminotransferase 89 IU/l (NR 10–55), alkaline phosphatase 109 IU/l (NR 30–130), and γ-glutamyltransferase 53 IU/L (NR 1–55), and serum albumin 27 g/l (NR 35–50). She had an erythrocyte sedimentation rate of 16 ml in first hour and immunoglobulins showed a pattern of hypogammaglobulinaemia with immunoglobulin G 2.56 g/l (NR 7–18.6), IgA 0.31 g/l (NR 0.78–4.8), and immuoglobulin M 0.2 g/l (NR 0.49–2). Serum protein electrophoresis showed a reduced gamma region and, urine measurement of Bence-Jones protein was negative. Routine ultrasonography to assess kidney size, and tests for Wegener's granulomatosis, systemic lupus erythamatosus, and antiglomerular basement membrane antibodies were negative. A diagnostic ascitic tap was performed, which showed an ascitic albumin of 8 g/l and a white cell count of 422 mm^3 (75% lymphocytes). Although this did not fulfil the definition of spontaneous bacterial peritonitis (> 250 polymorphs mm^3) it was felt that this represented partially treated spontaneous bacterial peritonitis from antibiotics given before transfer.

She was given piperacillin/tazobactam, linezolid, and amikacin, for sepsis and, she required noradrenaline for hypotension refractory to intravenous fluids. With the onset of grade II hepatic encephalopathy, a clinical diagnosis of SALF was made. She became oliguric, hypoxic, and hyperlactataemic (lactate 9 mmol/l, NR <2.5). She was intubated and ventilated, and continuous veno-venous haemofiltration was started. She was not listed as a candidate for emergency liver transplant because of concerns expressed in relation to the presence of an undiagnosed underlying malignant process. Her condition deteriorated further and she died on the 22nd day of her admission.

At necropsy the liver showed eosinophillic material that stained positive with Congo red, and displayed green birefringence when viewed under polarised light, confirming amyloid deposition (fig 1). Histological examination of the bone marrow showed a hypercellular pattern with diffuse infiltration of atypical plasmacytoid cells consistent with multiple myeloma (fig 2).

DISCUSSION

Hepatic failure as a consequence of amyloidosis and myeloma has been described before, but it is rare.[3 4] However, it has not been reported previously as presenting with SALF. This is, therefore, the first such case to have been reported in the English medical literature.

Abbreviations: SALF, subacute liver failure; ALF, acute liver failure

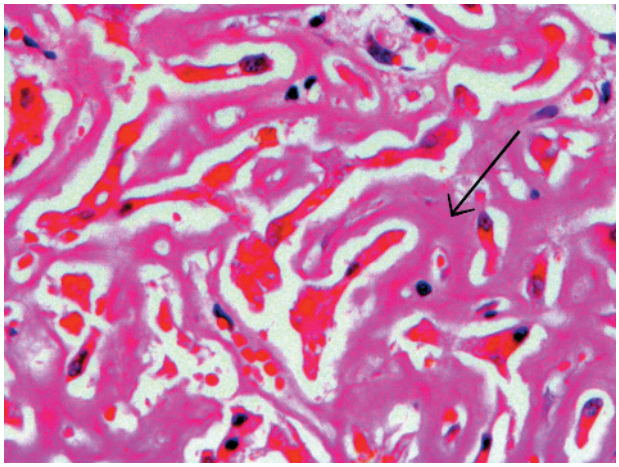

Figure 1 Liver biopsy (original magnification ×400). The hepatocyte plates are atrophied, and there is massive deposition of eosinophilic extracellular amyloid (arrow) along the sinusoids in the space of Disse.

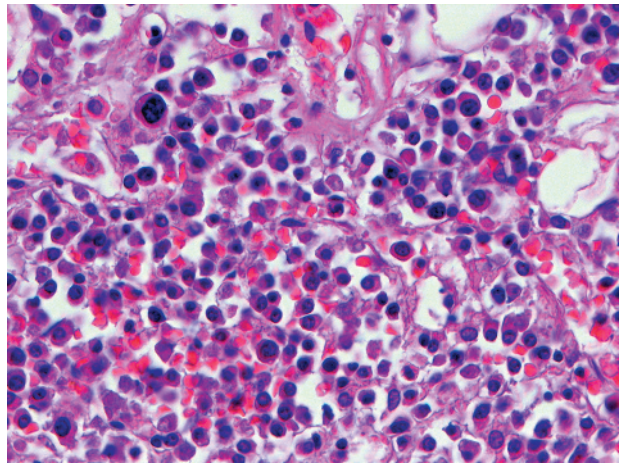

Figure 2 Bone marrow biopsy (original magnification ×400). An abnormal infiltrate consisting of variably sized, and cytologically atypical plasma cells replace the normal bone marrow. The histological features are those of myeloma.

Multiple myeloma is a malignant disease of plasma cells characterised by the presence of monoclonal protein in the blood or urine, bone marrow disease, and lytic bone lesions.[5] Investigations used to aid diagnosis include: full blood count, erythrocyte sedimentation rate, serum elctrophoresis, immunoglobulins, β-2 microglobulin, and serum free light chain assay. A full blood count may identify anaemia and low platelet count indicative of bone marrow involvement. Imaging studies comprise, a skeletal survey to identify lytic lesions, while computed tomography, magnetic resonance imaging, or positron emission scanning may identify plasmacytomas. Bone marrow aspiration and trephine is used to assess infiltration of plasma cells, and to assess marrow cellularity, morphology, and to permit cytogenetic analysis. In specialist centres serum amyloid protein scans may be used to determine amyloid load.

In this case the diagnosis was not immediately obvious for several reasons. Firstly, neither the erythrocyte sedimentation rate nor the total protein levels were raised. Furthermore, urinary Bence-Jones protein, which may be detectable in 20% of patients with light chain disease, was absent. Although, the presence of proteinuria may have suggested underlying amyloidosis, given the lack of obvious clues for myeloma this was overlooked. The presence of hypogammaglobulinaemia might have prompted us to consider immunoparesis and bone marrow infiltration, but the haematological parameters did not lead us to suspect bone marrow failure. Moreover, the patient's age also diverted us from a malignant process, as did the nature of the presentation. Despite the fact that liver involvement in malignancy is common, its presentation with ALF is rare. A study reviewing all admissions with ALF to a liver intensive care unit found that only 0.44% of cases were attributable to an infiltrating malignancy.[2] In these cases there was little to discriminate the usual presentations of ALF from malignancy, other than a longer prodrome for the latter.

The presence of liver involvement in multiple myeloma may manifest as abnormal hepatic biochemical parameters, hepatomegaly because of amyloid deposition, and cholestasis.[6] In addition jaundice because of hepatic myeloma infiltration, causing an extrahepatic obstructive jaundice, and because of pancreatic infiltration with myeloma have all been described.[7–10] In this case, the presence of a small liver consistent with a picture of SALF, added to the difficulty in reaching a diagnosis.

It is important to identify the cause of liver failure, given the nature of the diagnosis, to start appropriate treatment, and also prevent inappropriate listing for emergency liver transplant. The desire for liver transplant was in this case tempered by the rate of clinical deterioration of the patient.

In cases such as this, the diagnosis is best made by liver biopsy with or without bone marrow biopsy. While the complications from percutaneous liver biopsy are increased in the presence of coagulopathy, thrombocytopaenia, or both, the use of fresh frozen plasma and platelet transfusion may reduce these risks.[2] Furthermore, the use of a transjugular technique to obtain liver histology might prevent a major bleed. However, we did not do this in this particular case, because the risk-benefit ratio in a sick patient was considered low.

CONCLUSION

In conclusion, this case describes a patient with multiple myeloma associated amyloidosis, presenting with SALF. The erythrocyte sedimentation rate was not raisted, there was no monoclonal gammopathy, no detectable urinary Bence-Jones protein, and the liver was small. Clinicians should consider infiltrative disease, when patients present with a prolonged prodromal illness followed by unexplained worsening liver dysfunction. In such circumstances liver biopsy, with or without bone marrow examination, may be warranted. Emergency liver transplant in this context would be futile.

Learning points

- Malignant disease rarely presents with acute liver failure
- Emergency liver transplantation in the context of established malignancy is contraindicated.
- A diagnosis of infiltrating malignancy is best established with a liver biopsy with or without a bone marrow biopsy.
- Multiple myeloma can be associated with abnormal liver function because of amyloid deposition, or because of biliary obstruction or pancreatic head involvement.
- Spider naevi can be present in subacute liver failure, and are not only present in chronic liver disease.

Authors' affiliations
T J S Cross, J A Wendon, A Quaglia, M A Heneghan, P M Harrison, King's College London, Institute of Liver Studies, King's College Hospital, London, UK
J R Salisbury, Department of Histopathology, King's College Hospital

Funding: none.

Conflicts of interest: none.

Correspondence to: Dr T Cross, Institute of Liver Studies, Kings' College Hospital, London SE5 9RS, UK; tjscross@hotmail.com

Submitted 6 January 2006
Accepted 27 February 2006

REFERENCES

1 **O'Grady JG**, Schalm SW, Williams R. Acute liver failure: redefining the syndromes. Lancet, 1993;**342**:273–5.
2 **Rowbotham D**, Wendon J, Williams R. Acute liver failure secondary to hepatic infiltration: a single centre experience of 18 cases. *Gut* 1998;**42**:576–80.
3 **Yamamoto Y**, Maeda N, Kawasaki H. Hepatic failure in a case of multiple myeloma associated amyloidosis (κ-AL). *J Gastroenterol* 1995;**30**:393–7.
4 **Okabe M**, Choi GH, Kudo M, *et al*. Hepatic failure due to myeloma-associated amyloidosis. *J Gastroenterol* 1998;**33**:926–7.
5 **Sirohi B**, Powles R. Multiple myeloma. *Lancet* 2004;**363**:875–87.
6 **Perez-Saler R**, Esteban R, Allende E, *et al*. Liver involvement in multiple myeloma. *Am J Hematol* 1985;**20**:25–9.
7 **Arebi N**, Patel B, Aqel NM, *et al*. IgA multiple myeloma presenting as non-obstructive jaundice. *Postgrad Med J* 2004;**80**:489–90.
8 **Bell HG**, David R, Shamsuddin AM. Extrahepatic biliary obstruction and liver failure secondary to myeloma of the pancreas. *Hum Pathol* 1982;**3**:940–2.
9 **Abu-hammour AM**, Venu RP, Etzkom KP, *et al*. Common bile duct obstruction caused by multiple myeloma of the pancreas. *Gastrointest Endosc* 1996;**44**:606–8.
10 **Segev A**, Manor Y, Bernheim J, *et al*. Light chain myeloma presenting as severe obstructive jaundice due to hepatic amyloidosis. *Eur J Haematol* 1999;**63**:364–5.